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Access DB# CRFE

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Nirmal S. Basi Examiner # : _____ Date: 2/1/01
Art Unit: 1646 Phone Number 30_____ Serial Number: 09/273,217
Mail Box and Bldg/Room Location: CM1 10E17 Results Format Preferred (circle): PAPER DISK E-MAIL

10601

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Method for Identifying Specific ion channel Blockers.

Inventors (please provide full names): Yin-Yuan Cheng et al.

Earliest Priority Filing Date: 3/25/98

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search SEQ. ID NOS#: 1 through 4

Commercial + interference.

RUSH

All PRO

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STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher: B Smith	NA Sequence (#)_____		STN_____	
Searcher Phone #: 308-4477	AA Sequence (#) 4		Dialog_____	
Searcher Location: CM1-1E17	Structure (#)_____		Questel/Orbit_____	
Date Searcher Picked Up: 2/2/01	Bibliographic_____		Dr.Link_____	
Date Completed: 2/2/01	Litigation_____		Lexis/Nexis_____	
Searcher Prep & Review Time:_____	Fulltext_____		Sequence Systems 205504	
Clerical Prep Time: 5	Patent Family_____		WWW/Internet_____	
Online Time:_____	Other_____		Other (specify)_____	

PTO-1590 (1-2000)

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 ********** STN Columbus **********
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FILE 'MEDLINE'
FILE 'JAPIO'
FILE 'BIOSIS'
FILE 'SCISEARCH
FILE 'WPIDS'
FILE 'CAPLUS'
FILE 'EMBASE'
=> s ion channel#

L1    106710 ION CHANNEL#

=> s l1 and (kv1.2 or kv1.3 or kv3.1)

  5 FILES SEARCHED...
L2      479 L1 AND (KV1.2 OR KV1.3 OR KV3.1)

=> s l2 and antibod

=> s l2 and (antibody or antibodies)

L3       59 L2 AND (ANTIBODY OR ANTIBODIES)

=> dup rem l3

PROCESSING COMPLETED FOR L3
L4       34 DUP REM L3 (25 DUPLICATES REMOVED)

=> d l4 ibib abs 1-34


L4  ANSWER 1 OF 34  MEDLINE
DUPLICATE 1
ACCESSION NUMBER:  2000224145    MEDLINE
DOCUMENT NUMBER:  20224145
TITLE:           Brain insulin receptor causes
activity-dependent current
                 suppression in the olfactory bulb through multiple
                 phosphorylation of  ***Kv1*** . ***3*** .
AUTHOR:          Fadool D A; Tucker K; Phillips J J; Simmen
J A
CORPORATE SOURCE:  Department of Biological Sciences
and Program in
                 Neuroscience, Biomedical Research Facility,
Florida State
                 University, Tallahassee, Florida 32306, USA.
CONTRACT NUMBER:  R29DC-03387 (NIDCD)
SOURCE:          JOURNAL OF NEUROPHYSIOLOGY,
(2000 Apr) 83 (4) 2332-48.
                 Journal code: JC7. ISSN: 0022-3077.
PUB. COUNTRY:    United States
                 Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:        English
FILE SEGMENT:    Priority Journals
ENTRY MONTH:     200007
ENTRY WEEK:      20000703
AB  Insulin and insulin receptor (IR) kinase are found in
abundance in
    discrete brain regions yet insulin signaling in the CNS is not
understood.
    Because it is known that the highest brain insulin-binding
affinities,
    insulin-receptor density, and IR kinase activity are localized
to the
    olfactory bulb, we sought to explore the downstream
substrates for IR
    kinase in this region of the brain to better elucidate the
function of
    insulin signaling in the CNS. First, we demonstrate that IR is
postnatally
    and developmentally expressed in specific lamina of the
highly plastic
    olfactory bulb (OB). ELISA testing confirms that insulin is
present in the
    developing and adult OB. Plasma insulin levels are elevated
above that
    found in the OB, which perhaps suggests a differential
insulin pool.
    Olfactory bulb insulin levels appear not to be static,
however, but are
    elevated as much as 15-fold after a 72-h fasting period. Bath
application
    of insulin to cultured OB neurons acutely induces outward
current
    suppression as studied by the use of traditional whole-cell
and
    single-channel patch-clamp recording techniques.
Modulation of OB neurons
    is restricted to current magnitude; IR kinase activation does
not modulate
    current kinetics of inactivation or deactivation. Transient
transfection
    of human embryonic kidney cells with cloned  ***Kv1***
. ***3***
     ***ion***  ***channel*** , which carries a large
proportion of the
    outward current in these neurons, revealed that current
suppression was
    the result of multiple tyrosine phosphorylation of
***Kv1*** . ***3***
    channel. Y to F single-point mutations in the channel or
deletion of the
    kinase domain in IR blocks insulin-induced modulation and
phosphorylation
    of  ***Kv1*** . ***3*** . Neuromodulation of
***Kv1*** . ***3***
    current in OB neurons is activity dependent and is
eliminated after 20
    days of odor/sensory deprivation induced by unilateral naris
occlusion at
    postnatal day 1. IR kinase but not  ***Kv1*** . ***3***
expression is
    downregulated in the OB ipsilateral to the occlusion, as
demonstrated in
    cryosections of right (control) and left (sensory-deprived)
OB
    immunolabeled with  ***antibodies***  directed against
these proteins,
    respectively. Collectively, these data support the hypothesis
that the
    hormone insulin acts as a multiply functioning molecule in
the brain: IR
    signaling in the CNS could act as a traditional growth factor
during
    development, be altered during energy metabolism, and
simultaneously
    function to modulate electrical activity via phosphorylation
of
    voltage-gated  ***ion***  ***channels*** .

L4  ANSWER 2 OF 34  SCISEARCH  COPYRIGHT 2001 ISI
(R)
ACCESSION NUMBER:  2000:429499  SCISEARCH
THE GENUINE ARTICLE: 320FM
TITLE:           O-2-sensitive K+ channels: role of the
***Kv1*** .
                 ***2***  alpha-subunit in mediating the hypoxic
response
AUTHOR:          Conforti L (Reprint); Bodi I; Nisbet J W;
Millhorn D E
CORPORATE SOURCE:  UNIV CINCINNATI, DIV
NEPHROL & HYPERTENS, DEPT INTERNAL
                 MED, COLL MED, 231 BETHESDA AVE,
CINCINNATI, OH 45267
                 (Reprint); UNIV CINCINNATI, DEPT MOL &
CELLULAR PHYSIOL,
                 COLL MED, CINCINNATI, OH 45267; UNIV
CINCINNATI, INST MOL
                 PHARMACOL & BIOPHYS, COLL MED,
CINCINNATI, OH 45267
COUNTRY OF AUTHOR:  USA
SOURCE:          JOURNAL OF PHYSIOLOGY-LONDON,
(MAY 2000) Vol. 524, No. 3,
                 pp. 783-793.
                 Publisher: CAMBRIDGE UNIV PRESS, 40
WEST 20TH STREET, NEW
                 YORK, NY 10011-4211.
                 ISSN: 0022-3751.
DOCUMENT TYPE:   Article; Journal
FILE SEGMENT:    LIFE
LANGUAGE:        English
REFERENCE COUNT:  45
                 *ABSTRACT IS AVAILABLE IN THE ALL
AND IALL FORMATS*
AB  1. One of the early events in O-2 chemoreception is
inhibition of
    O-2-sensitive K+ (K-O2) channels. Characterization of the
molecular
    composition of the native K-O2 channels in chemosensitive
cells is
    important to understand the mechanism(s) that couple O-2
to the K-O2
    channels.
     2. The rat phaeochromocytoma PC12 clonal cell line
expresses an
    O-2-sensitive voltage-dependent K+ channel similar to that
recorded in
    other chemosensitive cells. Here we examine the possibility
that the
     ***Kv1*** . ***2***  alpha-subunit comprises the
K-O2 channel in PC12
    cells.
     3. Whole-cell voltage-clamp experiments showed that the
K-O2 current in
    PC12 cells is inhibited by charybdotoxin, a blocker of
***Kv1*** .
     ***2***  channels.
     4. PC12 cells express the  ***Kv1*** . ***2***
alpha-subunit of K+
    channels: Western blot analysis with affinity-purified anti-
***Kv1*** .
     ***2***  ***antibody***  revealed a band at similar to
80 kDa.
    Specificity of this  ***antibody***  was established in
Western blot and
    immunohystochemical studies. Anti-  ***Kv1*** .
***2***
     ***antibody***  selectively blocked  ***Kv1*** .
***2***  current
    expressed in the Xenopus oocyte, but had no effect on
Kv2.1 current.
     5. Anti-  ***Kv1*** . ***2***  ***antibody***
dialysed through
    the patch pipette completely blocked the K-O2 current,
while the
    anti-Kv2.1 and irrelevant  ***antibodies***  had no effect.
     6. The O-2 sensitivity of recombinant  ***Kv1*** .
***2***  and
    Kv2.1 channels was studied in Xenopus oocytes. Hypoxia
inhibited the
     ***Kv1*** . ***2***  current only.
     7. These findings show that the K-O2 channel in PC12
cells belongs to
    the Kv1 subfamily of K+ channels and that the
***Kv1*** . ***2***
    alpha-subunit is important in conferring O-2 sensitivity to
this channel.

L4  ANSWER 3 OF 34  SCISEARCH  COPYRIGHT 2001 ISI
(R)
ACCESSION NUMBER:  2000:925670  SCISEARCH
THE GENUINE ARTICLE: 378XM
TITLE:           KV1.1 K+ channels identification in human
breast carcinoma
                 cells: Involvement in cell proliferation
AUTHOR:          OuadidAhidouch H (Reprint); Chaussade
F; Roudbaraki M;
                 Slomianny C; Dewailly E; Delcourt P;
Prevarskaya N
CORPORATE SOURCE:  UNIV SCI & TECH LILLE
FLANDRES ARTOIS, INSERM, SN3, LAB
                 PHYSIOL CELLULAIRE, F-59655
VILLENEUVE DASCQ, FRANCE
                 (Reprint)
COUNTRY OF AUTHOR:  FRANCE
SOURCE:          BIOCHEMICAL AND BIOPHYSICAL
RESEARCH COMMUNICATIONS, (19
                 NOV 2000) Vol. 278, No. 2, pp. 272-277.
                 Publisher: ACADEMIC PRESS INC, 525 B ST,
STE 1900, SAN
                 DIEGO, CA 92101-4495.
                 ISSN: 0006-291X.
DOCUMENT TYPE:   Article; Journal
FILE SEGMENT:    LIFE
LANGUAGE:        English
REFERENCE COUNT:  30
                 *ABSTRACT IS AVAILABLE IN THE ALL
AND IALL FORMATS*
AB  Electrophysiological, immunocytochemical, and
RT-PCR methods were used
    to identify a K+ conductance not yet described in MCF-7
human breast
    cancer cells. A voltage-dependent and TEA-sensitive K+
current was the
    most commonly observed in these cells. The
noninactivating K+ current
    (I-K) was insensitive to iberiotoxin (100 nM) and
charybdotoxin (100 nM)
    but reduced by alpha -dendrotoxin (alpha -DTX). Perfusion
of (alpha -DTX
    reduced a fraction of I-K amplitude in a dose-dependent
manner (IC50 = 0.6
    +/- 0.3 nM). This DTX sensitive I-K exhibited a voltage
threshold at -20
    mV and was not inactivated. The time constant of activation
was 5.3 a 2.2
    ms measured at +60 mV. The averaged half-activation
potential and slope
    factor values were 14 +/- 1.6 mV and 10 +/- 1.4,
respectively.
    Immunocytochemical analysis demonstrated that plasma
membrane was labeled
    by anti-Kv1.1 but not by anti-  ***Kv1*** . ***2***  nor
anti-
     ***Kv1*** . ***3***  ***antibodies*** .
Furthermore, only Kv1.1 mRNA
    was detected in MCF-7 cells. Incubation in 1 and 10 nlM
alpha -DTX reduced
    cell proliferation by 20 and 30%, respectively. These data
provide the
    first evidence of Kv1.1 K+ channels expression in MCF-7
cells and indicate
    that these channels are implicated in cell proliferation. (C)
2000
    Academic Press.

L4  ANSWER 4 OF 34  BIOSIS  COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER:  2001:108835  BIOSIS
DOCUMENT NUMBER:  PREV200100108835
TITLE:           K+ channel expression in sensory neurons.
AUTHOR(S):       Rasband, M. N. (1); Park, E. W.; Trimmer,
J. S.
CORPORATE SOURCE:  (1) SUNY Stony Brook, Stony
Brook, NY USA
SOURCE:          Society for Neuroscience Abstracts, (2000)
Vol. 26, No.
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1-2, pp. Abstract No.-614.18. print.
Meeting Info.: 30th Annual Meeting of the Society of
Neuroscience New Orleans, LA, USA November 04-09, 2000
Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB To determine the K+ channels that are important in pain sensation, we have used a wide variety of K+ channel alpha (Kv1.1-6, Kv2.1-2, and Kv4.2-3) and beta (Kvbeta1-3) subunit specific monoclonal and polyclonal ***antibodies*** to determine the types of K+ channels present in rat dorsal root ganglia (DRG). Immunofluorescence staining and immunoblotting revealed that of the types tested, only Kv1.1, ***Kv1*** . ***2*** , Kv1.4, Kv1.6, and Kvbeta2 were present in DRG. Kv1.1, ***Kv1*** . ***2*** , and Kvbeta2 subunits were found primarily in large diameter neurons. Co-immunoprecipitation experiments showed that these subunits form heteromultimers in vivo. In contrast, ***antibodies*** against Kv1.4 specifically labeled small diameter neurons. Double-labeling of DRG sections for Na+ channels showed that the latter were highly expressed in small diameter neurons, and that this specific staining colocalized precisely with Kv1.4 immunoreactivity. ***Antibodies*** against VR-1 and calcitonin gene-related protein (CGRP) have been reported to label primarily small diameter, nociceptive neurons. We found that these also labeled mostly small diameter neurons in DRG with some Kv1.4 colocalization, but this was far less precisely correlated than that seen when DRG sections were double-labeled for Na+ channels. Our findings together with previous reports, both electrophysiological and immunocytochemical, suggest that Kv1.4 may be localized exclusively to small diameter nociceptive neurons and may be responsible for repolarization of these neurons following action potential conduction. As such, Kv1.4 may be useful as a therapeutic target to modulate peripheral pain. Supported by NIH NS34383, NS10906, and SCRF 2040.

L4 ANSWER 5 OF 34 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2000:36488 SCISEARCH
THE GENUINE ARTICLE: 270YC
TITLE: Recreation of neuronal Kv1 channel oligomers by expression in mammalian cells using Semliki Forest virus
AUTHOR: Shamotienko O; Akhtar S; Sidera C; Meunier F A; Ink B; Weir M; Dolly J O (Reprint)
CORPORATE SOURCE: UNIV LONDON IMPERIAL COLL SCI TECHNOL & MED, DEPT BIOCHEM, LONDON SW7 2AY, ENGLAND (Reprint); UNIV LONDON IMPERIAL COLL SCI TECHNOL & MED, DEPT BIOCHEM, LONDON SW7 2AY, ENGLAND; GLAXO WELLCOME RES & DEV LTD, STEVENAGE SG1 2NY, HERTS, ENGLAND
COUNTRY OF AUTHOR: ENGLAND
SOURCE: BIOCHEMISTRY, (21 DEC 1999) Vol. 38, No. 51, pp. 16766-16776.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
ISSN: 0006-2960.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 58
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The multiple roles of voltage-sensitive K+ channels (Kv1 subfamily) in brain are served by subtypes containing pore-forming alpha(1.1-1.6) and auxiliary beta subunits, usually in an (alpha)(4)(beta)(4) stoichiometry. To facilitate structure/activity analysis, combinations that are prevalent in neurones and susceptible to alpha-dendrotoxin (alpha DTX) were reproduced in mammalian cells, using Semliki Forest virus. Infected Chinese hamster ovary cells expressed N-glycosylated Kv1.1 and 1.2 alpha subunits (M-r similar to 60 and 62 K) that assembled and bound [I-125]-alpha DTX with high affinity; an appreciable proportion appeared on the cell surface, with ***Kv1*** . ***2*** showing a 5-fold enrichment in a plasma membrane fraction. To obtain 'native-like' alpha/beta complexes, beta 1.1 or 2.1 (M-r similar to 42 and 39 K, respectively) was co-expressed with Kv1.1 or 1.2. This slightly enhanced N-glycosylation and toxin binding, most notable with beta 2.1 and ***Kv1*** . ***2*** . Solubilization of membranes from cells infected with Kv.1.2 and beta 2.1, followed by Ni2+ chromatography, gave a purified alpha 1.2/beta 2.1 complex with a size of similar to 405 K and S-20,S-W = 15.8 S. Importantly, these values indicate that four alpha and beta subunits co-assembled as in neurones, a conclusion supported by the size (similar to 260 K) of the homo-tetramer formed by ***Kv1*** . ***2*** alone. Thus, an authentic K+ channel octomer has been reconstructed; oligomeric species were also found in plasma membranes. To create 'authentic-like' hetero-oligomeric channels, Kv1.1 and 1.2 were co-expressed and shown to have assembled by the precipitation of both with IgGs specific for either. Consistently, confocal microscopy of cells labeled with these ***antibodies*** showed that the relatively low surface content of Kv1.1 was increased by ***Kv1*** . ***2*** . [1-125]-alpha DTX binding to these complexes was antagonized by DTXk, a probe selective for Kv1.1, in a manner that mimicks the pattern observed for the Kv1.1/1.2-containing channels in neuronal membranes.

L4 ANSWER 6 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:92013 BIOSIS
DOCUMENT NUMBER: PREV200000092013
TITLE: K+ channel expression distinguishes subpopulations of parvalbumin- and somatostatin-containing neocortical interneurons.
AUTHOR(S): Chow, A.; Erisir, A.; Farb, C.; Nadal, M. S.; Ozaita, A.; Lau, D.; Welker, E.; Rudy, B. (1)
CORPORATE SOURCE: (1) Department of Physiology and Neuroscience, New York University School of Medicine, 550 First Avenue, New York, NY, 10016 USA
SOURCE: Journal of Neuroscience, (Nov. 1, 1999) Vol. 19, No. 21, pp. 9332-9345.
ISSN: 0270-6474.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB ***Kv3*** . ***1*** and Kv3.2 K+ channel proteins form similar voltage-gated K+ channels with unusual properties, including fast activation at voltages positive to -10 mV and very fast deactivation rates. These properties are thought to facilitate sustained high-frequency firing. ***Kv3*** . ***1*** subunits are specifically found in fast-spiking, parvalbumin (PV)-containing cortical interneurons, and recent studies have provided support for a crucial role in the generation of the fast-spiking phenotype. Kv3.2 mRNAs are also found in a small subset of neocortical neurons, although the distribution of these neurons is different. We raised ***antibodies*** directed against Kv3.2 proteins and used dual-labeling methods to identify the neocortical neurons expressing Kv3.2 proteins and to determine their subcellular localization. Kv3.2 proteins are prominently expressed in patches in somatic and proximal dendritic membrane as well as in axons and presynaptic terminals of GABAergic interneurons. Kv3.2 subunits are found in all PV-containing neurons in deep cortical layers where they probably form heteromultimeric channels with ***Kv3*** . ***1*** subunits. In contrast, in superficial layer PV-positive neurons Kv3.2 immunoreactivity is low, but ***Kv3*** . ***1*** is still prominently expressed. Because ***Kv3*** . ***1*** and Kv3.2 channels are differentially modulated by protein kinases, these results raise the possibility that the fast-spiking properties of superficial- and deep-layer PV neurons are differentially regulated by neuromodulators. Interestingly, Kv3.2 but not ***Kv3*** . ***1*** proteins are also prominent in a subset of seemingly non-fast-spiking, somatostatin- and calbindin-containing interneurons, suggesting that the ***Kv3*** . ***1*** -Kv3.2 current type can have functions other than facilitating high-frequency firing.

L4 ANSWER 7 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:491199 BIOSIS
DOCUMENT NUMBER: PREV199900491199
TITLE: ***Kv3*** . ***1*** -Kv3.2 channels underlie a high-voltage-activating component of the delayed rectifier K+ current in projecting neurons from the globus pallidus.
AUTHOR(S): Hernandez-Pineda, R.; Chow, A.; Amarillo, Y.; Moreno, H.; Saganich, M.; de Miera, E. Vega-Saenz; Hernandez-Cruz, A.; Rudy, B. (1)
CORPORATE SOURCE: (1) Dept. of Physiology and Neuroscience, New York University School of Medicine, 550 First Ave., New York City, NY, 10016 USA
SOURCE: Journal of Neurophysiology (Bethesda), (Sept., 1999) Vol. 82, No. 3, pp. 1512-1528.
ISSN: 0022-3077.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The globus pallidus plays central roles in the basal ganglia circuitry involved in movement control as well as in cognitive and emotional functions. There is therefore great interest in the anatomic and electrophysiological characterization of this nucleus. Most pallidal neurons are GABAergic projecting cells, a large fraction of which express the calcium binding protein parvalbumin (PV). Here we show that PV-containing pallidal neurons coexpress ***Kv3*** . ***1*** and Kv3.2 K+ channel proteins and that both ***Kv3*** . ***1*** and Kv3.2 ***antibodies*** coprecipitate both channel proteins from pallidal membrane extracts solubilized with nondenaturing detergents, suggesting that the two channel subunits are forming heteromeric channels. ***Kv3*** . ***1*** and Kv3.2 channels have several unusual electrophysiological properties when expressed in heterologous expression systems and are thought to play special roles in neuronal excitability including facilitating sustained high-frequency firing in fast-spiking neurons such as interneurons in the cortex and the hippocampus. Electrophysiological analysis of freshly dissociated pallidal neurons demonstrates that these cells have a current that is nearly identical to the currents expressed by ***Kv3*** . ***1*** and Kv3.2 proteins in heterologous expression systems, including activation at very depolarized membrane potentials (more positive than - 10 mV) and very

fast
deactivation rates. These results suggest that the electrophysiological
properties of native channels containing ***Kv3*** . ***1*** and
Kv3.2 proteins in pallidal neurons are not significantly affected by
factors such as associated subunits or postranslational modifications that
result in channels having different properties in heterologous expression
systems and native neurons. Most neurons in the globus pallidus have been
reported to fire sustained trains of action potentials at high-frequency.
Kv3 . ***1*** -Kv3.2 voltage-gated K+ channels may play a role in
helping maintain sustained high-frequency repetitive firing as they
probably do in other neurons.

L4 ANSWER 8 OF 34 MEDLINE
ACCESSION NUMBER: 2000088303 MEDLINE
DOCUMENT NUMBER: 20088303
TITLE: Caspr2, a new member of the neurexin superfamily, is
localized at the juxtaparanodes of myelinated axons and
associates with K+ channels.
AUTHOR: Poliak S; Gollan L; Martinez R; Custer A; Einheber S;
Salzer J L; Trimmer J S; Shrager P; Peles E
CORPORATE SOURCE: Department of Molecular Cell Biology, The Weizmann
Institute of Science, Rehovot, Israel.
CONTRACT NUMBER: NS17965 (NINDS)
NS38208 (NINDS)
NS34383 (NINDS)
SOURCE: NEURON, (1999 Dec) 24 (4) 1037-47.
Journal code: AN8. ISSN: 0896-6273.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF193613
ENTRY MONTH: 200003
ENTRY WEEK: 20000305
AB Rapid conduction in myelinated axons depends on the generation of
specialized subcellular domains to which different sets of ***ion***
channels are localized. Here, we describe the identification of
Caspr2, a mammalian homolog of Drosophila Neurexin IV (Nrx-IV), and show
that this neurexin-like protein and the closely related molecule
Caspr/Paranodin demarcate distinct subdomains in myelinated axons. While
contactin-associated protein (Caspr) is present at the paranodal
junctions, Caspr2 is precisely colocalized with Shaker-like K+ channels in
the juxtaparanodal region. We further show that Caspr2 specifically
associates with Kv1.1, ***Kv1*** . ***2*** , and their Kvbeta2
subunit. This association involves the C-terminal sequence of Caspr2,
which contains a putative PDZ binding site. These results suggest a role
for Caspr family members in the local differentiation of the axon into
distinct functional subdomains.

L4 ANSWER 9 OF 34 MEDLINE
ACCESSION NUMBER: 1999270675 MEDLINE
DOCUMENT NUMBER: 99270675
TITLE: ***Antibodies*** against Tityus discrepans venom do not
abolish the effect of Tityus serrulatus venom on the rat
sodium and potassium channels.
AUTHOR: Borges A; Tsushima R G; Backx P H
CORPORATE SOURCE: Departamento de Biologia Celular, Universidad Simon
Bolivar, Sartenejas, Caracas, Venezuela..
aborges@mailexcite.com
SOURCE: TOXICON, (1999 Jun) 37 (6) 867-81.
Journal code: VWT. ISSN: 0041-0101.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY WEEK: 19990902
AB Anti-(Tityus serrulatus + Tityus bahiensis) and anti-Tityus discrepans
venom polyclonal antisera were used to investigate whether antigenic
differences exist between the venoms of the Brazilian T. serrulatus and
the Venezuelan T. discrepans scorpions. Both antisera recognised the
toxin-containing electrophoretic fractions of their cognate venoms and
also those from Tityus zulianus and Tityus trinitatis venoms on Western
blots. The anti-T. discrepans antiserum reacted only weakly with T.
serrulatus toxic polypeptides. The effect of T. serrulatus alpha- or
beta-toxins on rat skeletal muscle Na+ channels expressed in Xenopus
laevis oocytes was abolished by pre-incubating the venom with anti-(T.
serrulatus + T. bahiensis) serum but not with anti-T. discrepans serum.
Nor did the Brazilian or the Venezuelan sera prevent the reduction in K+
currents by T. serrulatus venom in X. laevis oocytes expressing the rat
brain delayed rectifying Shaker K+ channel (***Kv1*** . ***2***).
These results indicate that toxins from T. serrulatus and T. discrepans
venoms, which primarily target mammalian Na+ channels, are antigenically
distinct, although they probably share common epitopes. Our results also
suggest that Na+ channel-active toxins are the immunodominant antigens of
the T. serrulatus venom.

L4 ANSWER 10 OF 34 CAPLUS COPYRIGHT 2001 ACS
DUPLICATE 2
ACCESSION NUMBER: 1999:401935 CAPLUS
DOCUMENT NUMBER: 131:53477
TITLE: The therapeutic potential for targetting potassium
channels. Are dendrotoxins a suitable basis for drug
design?
AUTHOR(S): Harvey, Alan L.; Dufton, Mark J.
CORPORATE SOURCE: Department Physiology Pharmacology, Institute Drug
Research, Univ. Strathclyde, Glasgow, G1 1XW, UK
SOURCE: Perspect. Drug Discovery Des. (1999), 15/16(Animal
Toxins and Potassium Channels), 281-294
CODEN: PDDDEC; ISSN: 0928-2866
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review is given with 51 refs. Voltage-dependent K ***ion***
channels were implicated in several diseases of genetic or
autoimmune origin. There are genetic defects of specific K channel genes
in episodic ataxia with myokymia, long QT syndrome, Jervell-Lange-Nielsen
syndrome, and familial hyperinsulinemic hypoglycemia of infancy.
Antibodies against voltage-gated K channels were detected in
Isaacs syndrome (acquired neuromyotonia). Voltage-gated K channels were
also regarded as therapeutic targets for immunosuppressants (targeting
Kv1 . ***3*** channels) and in some neurodegenerative diseases
(targeting Kv1.1 or 1.2 channels). Specific blockers of K channels may be
designed from an understanding of the mol. recognition properties of
highly specific K channel blocking toxins such as dendrotoxin. The
dendrotoxin family of toxins and their genetic relatives in the Kunitz
family of proteinase inhibitors were studied extensively in recent years.
Structural studies and functional studies with mutated toxins provide
information that should help the rational design of analogs with the
desired properties.
REFERENCE COUNT: 51
REFERENCE(S): (1) Adelman, J; Neuron 1995, V15, P1449 CAPLUS
(2) Agostinho, P; Bioelectrochem Bioenergetics 1995,
V38, P297 CAPLUS
(4) Bagetta, G; Neurochem Int 1994, V24, P81 CAPLUS
(5) Bandmann, O; Neuroscience 1996, V72, P877 CAPLUS
(6) Barhanin, J; Nature 1996, V384, P78 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 34 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:451849 SCISEARCH
THE GENUINE ARTICLE: 203PJ
TITLE: The therapeutic potential for targetting potassium
channels: Are dendrotoxins a suitable basis for drug
design?
AUTHOR: Harvey A L (Reprint); Dufton M J
CORPORATE SOURCE: UNIV STRATHCLYDE, DEPT PHYSIOL & PHARMACOL, GLASGOW G1
1XW, LANARK, SCOTLAND (Reprint); UNIV STRATHCLYDE,
STRATHCLYDE INST DRUG RES, DEPT PURE & APPL CHEM, GLASGOW
G1 1XW, LANARK, SCOTLAND
COUNTRY OF AUTHOR: SCOTLAND
SOURCE: PERSPECTIVES IN DRUG DISCOVERY AND DESIGN, (MAY 1999) Vol.
16, pp. 281-294.
Publisher: KLUWER ACADEMIC PUBL, SPUIBOULEVARD 50, PO BOX
17, 3300 AA DORDRECHT, NETHERLANDS.
ISSN: 0928-2866.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 51
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Voltage-dependent potassium ***ion*** ***channels*** have been
implicated in several diseases of genetic or autoimmune origin. There are
genetic defects of specific potassium channel genes in episodic ataxia
with myokymia, long QT syndrome, Jervell-Lange-Nielsen syndrome, and
familial hyperinsulinemic hypoglycemia of infancy. ***Antibodies***
against voltage-gated potassium channels have been detected in Isaacs
syndrome (acquired neuromyotonia). Voltage-gated potassium channels have
also been regarded as therapeutic targets for immunosuppressants
(targetting ***Kv1*** . ***3*** channels) and in some neurodegenerative diseases (targetting Kv1.1 or 1.2 channels). Specific
blockers of potassium channels may be designed from an understanding of
the molecular recognition properties of highly specific potassium channel
blocking toxins such as dendrotoxin. The dendrotoxin family of toxins and
their genetic relatives in the Kunitz family of proteinase inhibitors have
been studied extensively in recent years. Structural studies and
functional studies with mutated toxins provide information that should
help the rational design of analogues with the desired properties.

L4 ANSWER 12 OF 34 MEDLINE
DUPLICATE 3
ACCESSION NUMBER: 1999270588 MEDLINE
DOCUMENT NUMBER: 99270588
TITLE: Voltage-gated sodium and potassium channels in radial glial
cells of trout optic tectum studied by patch clamp analysis
and single cell RT-PCR.
AUTHOR: Rabe H; Koschorek E; Nona S N; Ritz H J; Jeserich G
CORPORATE SOURCE: Abteilung Zoophysiologie, Universitat Osnabruck, Germany.
SOURCE: GLIA, (1999 May) 26 (3) 221-32.
Journal code: GLI. ISSN: 0894-1491.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY WEEK: 19991001
AB Radial glial cells in the visual center of trout were analyzed
immunocytochemically and with the whole cell mode of the patch-clamp
technique in combination with RT-PCR. By immunostaining with anti-GFAP
antibodies radially oriented cell processes spanning the entire
width of the tectum were brightly labeled, while with anti-S-100 antiserum
the cell bodies residing in a discrete layer close to the

ventricular
border became most clearly visible. Virtually all radial glial cells
examined in brain slices exhibited voltage-gated sodium inward currents
that were activated above -40 mV, blocked by micromolar concentrations of
TTX and totally eliminated if sodium was substituted for Tris in the bath
solution. In contrast with adjacent nerve cells of the same slices radial
glial cells did not exhibit spontaneous electrical activity and could not
be stimulated to generate action potentials by depolarizing current
injections. Two types of voltage-gated potassium outward currents were
elicited by depolarizing voltage steps: a sustained current with delayed
rectifier properties and a superimposed transient "A"-type current, both
being activated at a threshold potential of -40 mV. In cultured radial
glial cells subtle differences were noticed regarding current density,
inactivation kinetics, and TEA-sensitivity of the potassium currents.
Inwardly rectifying potassium currents activating at hyperpolarized
voltages were not observed. By single cell RT-PCR the transcripts of two
shaker-related potassium channel genes (termed tsha1-a fish homologue to
Kv1 . ***2*** - and tsha3) were amplified, while transcripts for
tsha 2 and tsha 4 were not detected.

L4 ANSWER 13 OF 34 MEDLINE
DUPLICATE 4
ACCESSION NUMBER: 1998112806 MEDLINE
DOCUMENT NUMBER: 98112806
TITLE: Subunit composition of brain voltage-gated potassium
channels determined by hongotoxin-1, a novel peptide
derived from Centruroides limbatus venom.
AUTHOR: Koschak A; Bugianesi R M; Mitterdorfer J; Kaczorowski G J;
Garcia M L; Knaus H G
CORPORATE SOURCE: Institute for Biochemical Pharmacology, University of
Innsbruck, Peter-Mayr Strasse 1, A-6020 Innsbruck, Austria.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Jan 30) 273 (5)
2639-44.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199804
ENTRY WEEK: 19980404
AB Five novel peptidyl inhibitors of Shaker-type (Kv1) K+ channels have been
purified to homogeneity from venom of the scorpion Centruroides limbatus.
The complete primary amino acid sequence of the major component,
hongotoxin-1 (HgTX1), has been determined and confirmed after expression
of the peptide in Escherichia coli. HgTX1 inhibits 125I-margatoxin binding
to rat brain membranes as well as depolarization-induced 86Rb+ flux
through homotetrameric Kv1.1, ***Kv1*** . ***2*** , and ***Kv1***
. ***3*** channels stably transfected in HEK-293 cells, but it displays
much lower affinity for Kv1.6 channels. A HgTX1 double mutant
(HgTX1-A19Y/Y37F) was constructed to allow high specific activity
iodination of the peptide. HgTX1-A19Y/Y37F and monoiodinated
HgTX1-A19Y/Y37F are equally potent in inhibiting 125I-margatoxin binding
to rat brain membranes as HgTX1 (IC50 values approximately 0.3 pM).
125I-HgTX1-A19Y/Y37F binds with subpicomolar affinities to membranes
derived from HEK-293 cells expressing homotetrameric Kv1.1, ***Kv1***
2 , and ***Kv1*** . ***3*** channels and to rat brain
membranes (Kd values 0.1-0.25 pM, respectively) but with lower affinity to
Kv1.6 channels (Kd 9.6 pM), and it does not interact with either Kv1.4 or
Kv1.5 channels. Several subpopulations of native Kv1 subunit oligomers
that contribute to the rat brain HgTX1 receptor have been deduced by
immunoprecipitation experiments using ***antibodies*** specific for
Kv1 subunits. HgTX1 represents a novel and useful tool with which to
investigate subclasses of voltage-gated K+ channels and Kv1 subunit
assembly in different tissues.

L4 ANSWER 14 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:52825 BIOSIS
DOCUMENT NUMBER: PREV199900052825
TITLE: Early expression of a novel K+ current in rat microglia.
AUTHOR(S): Kotecha, S. A. (1); Schlichter, L. C.
CORPORATE SOURCE: (1) Univ. Toronto, Dep. Physiol., Toronto, ON Canada
SOURCE: Society for Neuroscience Abstracts, (1998) Vol. 24, No.
1-2, pp. 830.
Meeting Info.: 28th Annual Meeting of the Society for
Neuroscience, Part 1 Los Angeles, California, USA November
7-12, 1998 Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English

L4 ANSWER 15 OF 34 MEDLINE
DUPLICATE 5
ACCESSION NUMBER: 1998190097 MEDLINE
DOCUMENT NUMBER: 98190097
TITLE: Specific ***antibodies*** to the external vestibule of
voltage-gated potassium channels block current.
AUTHOR: Zhou B Y; Ma W; Huang X Y
CORPORATE SOURCE: Department of Physiology, Cornell University Medical
College, New York 10021, USA.
SOURCE: JOURNAL OF GENERAL PHYSIOLOGY, (1998 Apr) 111 (4) 555-63.
Journal code: I8N. ISSN: 0022-1295.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY WEEK: 19980701
AB Using delayed-rectifier potassium channels as examples, we have designed
two specific blockers by generating specific antipeptide
antibodies to epitopes in the external vestibules of two channel
proteins, ***Kv1*** . ***2*** and ***Kv3*** .
1 . These
antibodies reduced whole-cell ***Kv1*** .
2 or
Kv3 . ***1*** currents in transfected cells and the effect was
blocked by the corresponding peptide antigen, but not by control peptides.
A control ***antibody*** had little effect on
Kv1 . ***2***
currents and the ***Kv1*** . ***2*** blocker
antibody had
limited effect on other related potassium currents. Furthermore, the
Kv1 . ***2*** blocking ***antibody***
inhibited dendrotoxin
binding to ***Kv1*** . ***2*** channel proteins in transfected
cells. Moreover, using the ***Kv1*** . ***2***
blocker
antibody , we determined the presence and relative contribution of
endogenous ***Kv1*** . ***2*** to the overall endogenous K+ currents
in NG108 neuronal cells. This guided design of specific channel blockers
will facilitate future physiological studies on ***ion***
channel functions.

L4 ANSWER 16 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:311628 BIOSIS
DOCUMENT NUMBER: PREV199800311628
TITLE: Differential distribution of Shaker-like and Shab-like
K+-channel subunits in goldfish retina and retinal bipolar
cells.
AUTHOR(S): Yazulla, Stephen (1); Studholme, Keith M.
CORPORATE SOURCE: (1) Dep. Neurobiol. Behavior, Univ. Stony Brook, Stony
Brook, NY 11794-5230 USA
SOURCE: Journal of Comparative Neurology, (June 22, 1998) Vol. 396,
No. 1, pp. 131-140.
ISSN: 0021-9967.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The distributions of Shaker subfamily Kv1.1 and ***Kv1*** . ***2***
and Shab subfamily Kv2.1 subunits of voltage-gated K+ channels were
determined in the retina and ON bipolar cells of goldfish by using
double-label light and electron microscopic immunocytochemistry. All
labeling to be described was blocked by preabsorption of the primary
antibodies with antigen. The retina was labeled throughout with
all three ***antibodies*** . However, labeling was densest in the inner
plexiform layer for Kv1.1, more concentrated in the outer nuclear layer
for Kv2.1, and uniform throughout for ***Kv1*** .
2 . All ON
mixed rod/cone (mb) and cone (cb) bipolar somata and the proximal portions
of their axons and dendrites were labeled for anti-Kv1.1, ***Kv1*** .
2 , and Kv2.1. Labeling of axons rarely extended over the mb axon
terminal. Only ***Kv1*** . ***2***
antibodies labeled mb
bipolar cell dendrites in the outer plexiform layer. No evidence for
Kv1.1, 1.2, or 2.1 ***antibody*** labeling of OFF bipolar cells was
found. Ultrastructurally, ***Kv1*** . ***2***
-immunoreactivity was
associated with the plasma membrane of bipolar cell bodies and with
dendrites that make narrow-cleft junctions with cone terminals (ON-type).
Kv immunoreactivity was not found associated with presynaptic membranes in
the inner plexiform layer and was found only rarely with membranes,
postsynaptic to an amacrine cell process. Although both Shaker and Shab
subfamilies include delayed rectifiers, their activation properties
differ, suggesting differential modulation of K+ conductances in bipolar
cells based not only on the presence or absence of rod photoreceptor input
but also whether the bipolar cells are of the ON or OFF type.

L4 ANSWER 17 OF 34 MEDLINE
ACCESSION NUMBER: 1998010587 MEDLINE
DOCUMENT NUMBER: 98010587
TITLE: Complex subunit assembly of neuronal voltage-gated K+
channels. Basis for high-affinity toxin interactions and
pharmacology.
AUTHOR: Koch R O; Wanner S G; Koschak A; Hanner M; Schwarzer C;
Kaczorowski G J; Slaughter R S; Garcia M L; Knaus H G
CORPORATE SOURCE: Institute for Biochemical Pharmacology, Neuropharmacology
Unit, University Innsbruck, Peter-Mayr Strasse 1, A-6020
Innsbruck, Austria.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Oct 31) 272 (44)
27577-81.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199802
ENTRY WEEK: 19980204
AB Neurons require specific patterns of K+ channel subunit expression as well
as the precise coassembly of channel subunits into heterotetrameric
structures for proper integration and transmission of electrical signals.
In vivo subunit coassembly was investigated by studying the
pharmacological profile, distribution, and subunit composition of
voltage-gated Shaker family K+ (Kv1) channels in rat cerebellum that are
labeled by 125I-margatoxin (125I-MgTX; Kd, 0.08 pM). High-resolution
receptor autoradiography showed spatial receptor expression mainly in
basket cell terminals (52% of all cerebellar sites) and the molecular
layer (39% of sites). Sequence-directed ***antibodies***

indicated
overlapping expression of Kv1. 1 and ***Kv1*** . ***2*** in basket
cell terminals, whereas the molecular layer expressed Kv1.1, ***Kv1***
. ***2*** , ***Kv1*** . ***3*** , and Kv1.6 proteins.
Immunoprecipitation experiments revealed that all 125I-MgTX receptors
contain at least one ***Kv1*** . ***2*** subunit and that 83% of
these receptors are heterotetramers of Kv1.1 and ***Kv1*** . ***2***
subunits. Moreover, 33% of these Kv1.1/ ***Kv1*** . ***2***
-containing receptors possess either an additional ***Kv1*** . ***3***
or Kv1.6 subunit. Only a minority of the 125I-MgTX receptors (<20%) seem
to be homotetrameric ***Kv1*** . ***2*** channels. Heterologous
coexpression of Kv1.1 and ***Kv1*** . ***2*** subunits in COS-1
cells leads to the formation of a complex that combines the
pharmacological profile of both parent subunits, reconstituting the native
MgTX receptor phenotype. Subunit assembly provides the structural basis
for toxin binding pharmacology and can lead to the association of as many
as three distinct channel subunits to form functional K+ channels in vivo.

L4 ANSWER 18 OF 34 MEDLINE
ACCESSION NUMBER: 1998060804 MEDLINE
DOCUMENT NUMBER: 98060804
TITLE: Evidence for interaction between transmembrane segments in
assembly of ***Kv1*** . ***3*** .
AUTHOR: Sheng Z; Skach W; Santarelli V; Deutsch C
CORPORATE SOURCE: Department of Physiology, University of Pennsylvania,
Philadelphia, Pennsylvania 19104-6085, USA.
CONTRACT NUMBER: GM52302 (NIGMS)
GM53457 (NIGMS)
SOURCE: BIOCHEMISTRY, (1997 Dec 9) 36 (49) 15501-13.
Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY WEEK: 19980302
AB Previously, we showed that the N-terminal recognition domain (T1) of
Kv1 . ***3*** was not required for assembly of functional
channels [Tu et al. (1996) J. Biol. Chem. 271, 18904-18911]. Moreover,
specific ***Kv1*** . ***3*** peptide fragments including regions of
the central core are able to inhibit expression of current produced from a
channel lacking the T1 domain, ***Kv1*** . ***3*** (T1-). To
elucidate the mechanism whereby ***Kv1*** . ***3*** peptide
fragments suppress ***Kv1*** . ***3*** (T1-) current, we have studied
the ability of peptide fragments containing the transmembrane segments S1,
S1-S2, or S1-S2-S3 to physically associate with the ***Kv1*** .
3 (T1-) polypeptide subunit in vitro in microsomal membranes. Using
c-myc (9E10) epitope-labeled peptide fragments and anti-myc
antibody as well as antisera to the ***Kv1*** .
3
C-terminus, we now demonstrate specific association of these peptide
fragments with ***Kv1*** . ***3*** (T1-). Association of peptide
fragments with ***Kv1*** . ***3*** (T1-) was correlated with
integration of both proteins into the membrane. Furthermore, the relative
strength and kinetics of this association directly correlated with the
ability of fragments to suppress ***Kv1*** . ***3*** (T1-) current.
The rate-limiting step in the sequential synthesis, integration, and
formation of a complex was the association of integrated polypeptides
within the plane of the lipid bilayer. These results strongly suggest that
the physical association of transmembrane segments provides the basis for
suppression of K+ channel function by K+ channel peptide fragments in
vivo. Moreover, the S1-S2-S3 peptide fragment potently suppressed
full-length ***Kv1*** . ***3*** , thus implicating a role for the
S1-S2-S3 region of ***Kv1*** . ***3*** in the assembly of the
Kv1 . ***3*** channel. We refer to these putative association
sites as IMA (intramembrane association) sites.

L4 ANSWER 19 OF 34 SCISEARCH COPYRIGHT 2001 ISI (R) DUPLICATE 6
ACCESSION NUMBER: 97:810121 SCISEARCH
THE GENUINE ARTICLE: YC947
TITLE: Association and colocalization of the Kv beta 1 and Kv
beta 2 beta-subunits with Kv1 alpha-subunits in mammalian
brain K+ channel complexes
AUTHOR: Rhodes K J; Strassle B W; Monaghan M M; BekeleArcuri Z;
Matos M F; Trimmer J S (Reprint)
CORPORATE SOURCE: SUNY STONY BROOK, DEPT BIOCHEM & CELL BIOL, STONY BROOK,
NY 11794 (Reprint); SUNY STONY BROOK, DEPT BIOCHEM & CELL
BIOL, STONY BROOK, NY 11794; SUNY STONY BROOK, INST CELL &
DEV BIOL, STONY BROOK, NY 11794; WYETH AYERST RES, CENT
NERVOUS SYST DISORDERS, PRINCETON, NJ 08543
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF NEUROSCIENCE, (1 NOV 1997) Vol. 17, No. 21, pp.
8246-8258.
Publisher: SOC NEUROSCIENCE, 11 DUPONT CIRCLE, NW, STE
500, WASHINGTON, DC 20036.
ISSN: 0270-6474.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 45
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The differential expression and association of cytoplasmic
beta-subunits with pore-forming alpha-subunits may contribute
significantly to the complexity and heterogeneity of voltage-gated K+
channels in excitable cells. Here we examined the association and
colocalization of two mammalian beta-subunits, Kv beta 1 and Kv beta 2,
with the K+ channel alpha-subunits Kv1.1, ***Kv1*** . ***2*** ,
Kv1.4, Kv1.6, and Kv2.1 in adult rat brain. Reciprocal
coimmunoprecipitation experiments using subunit-specific
antibodies indicated that Kv beta 1 and Kv beta 2 associate with
all the Kv1 alpha-subunits examined, and with each other, but not with
Kv2.1. A much larger portion of the total brain pool of Kv1-containing
channel complexes was found associated with Kv beta 2 than with Kv beta 1.
Single- and multiple-label immunohistochemical staining indicated that Kv
beta 1 codistributes extensively with Kv1.1 and Kv1.4 in cortical
interneurons, in the hippocampal perforant path and messy fiber pathways,
and in the globus pallidus and substantia nigra. Kv beta 2 codistributes
extensively with Kv1.1 and ***Kv1*** . ***2*** in all brain regions
examined and was strikingly colocalized with these alpha-subunits in the
juxtaparanodal region of nodes of Ranvier as well as in the axons and
terminals of cerebellar basket cells. Taken together, these data provide a
direct demonstration that Kv beta 1 and Kv beta 2 associate and colocalize
with Kv1 alpha-subunits in native tissues and provide a biochemical and
neuroanatomical basis for the differential contribution of Kv1 alpha- and
beta-subunits to electrophysiologically diverse neuronal K+ currents.

L4 ANSWER 20 OF 34 MEDLINE
DUPLICATE 7
ACCESSION NUMBER: 97454368 MEDLINE
DOCUMENT NUMBER: 97454368
TITLE: Tyrosine phosphorylation modulates current amplitude and
kinetics of a neuronal voltage-gated potassium channel.
AUTHOR: Fadool D A; Holmes T C; Berman K; Dagan D; Levitan I B
CORPORATE SOURCE: Department of Biochemistry and Volen Center for Complex
Systems, Brandeis University, Waltham, Massachusetts 02254,
USA.
SOURCE: JOURNAL OF NEUROPHYSIOLOGY, (1997 Sep) 78 (3) 1563-73.
Journal code: JC7. ISSN: 0022-3077.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
AB The modulation of the ***Kv1*** . ***3*** potassium channel by
tyrosine phosphorylation was studied. ***Kv1*** . ***3*** was
expressed in human embryonic kidney (HEK 293) cells, and its activity was
measured by cell-attached patch recording. The amplitude of the
characteristic C-type inactivating ***Kv1*** . ***3*** current is
reduced by >95%, in all cells tested, when the channel is co-expressed
with the constitutively active nonreceptor tyrosine kinase, v-Src. This
v-Src-induced suppression of current is accompanied by a robust tyrosine
phosphorylation of the channel protein. No suppression of current or
tyrosine phosphorylation of ***Kv1*** . ***3*** protein is observed
when the channel is co-expressed with R385A v-Src, a mutant with severely
impaired tyrosine kinase activity. v-Src-induced suppression of
Kv1 . ***3*** current is relieved by pretreatment of the HEK 293
cells with two structurally different tyrosine kinase inhibitors,
herbimycin A and genistein. Furthermore, ***Kv1*** . ***3*** channel
protein is processed properly and targeted to the plasma membrane in v-Src
cotransfected cells, as demonstrated by confocal microscopy using an
antibody directed against an extracellular epitope on the channel.
Thus v-Src-induced suppression of ***Kv1*** . ***3*** current is not
mediated through decreased channel protein expression or interference with
its targeting to the plasma membrane. v-Src co-expression also slows the
C-type inactivation and speeds the deactivation of the residual
Kv1 . ***3*** current. Mutational analysis demonstrates that
each of these modulatory changes, in current amplitude and kinetics,
requires the phosphorylation of ***Kv1*** . ***3*** at multiple
tyrosine residues. Furthermore, a different combination of tyrosine
residues is involved in each of the modulatory changes. These results
emphasize the complexity of signal integration at the level of a single
ion ***channel*** .

L4 ANSWER 21 OF 34 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 97:842775 SCISEARCH
THE GENUINE ARTICLE: YF133
TITLE: Modulation of the ***Kv1*** . ***3*** potassium
channel by receptor tyrosine kinases
AUTHOR: Bowlby M R; Fadool D A; Holmes T C; Levitan I B (Reprint)
CORPORATE SOURCE: BRANDEIS UNIV, VOLEN CTR COMPLEX SYST, WALTHAM, MA 02254
(Reprint); BRANDEIS UNIV, VOLEN CTR COMPLEX SYST, WALTHAM,
MA 02254; BRANDEIS UNIV, DEPT BIOCHEM, WALTHAM, MA 02254
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF GENERAL PHYSIOLOGY, (NOV 1997) Vol. 110, No. 5,
pp. 601-610.
Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL,
NEW YORK, NY 10021.
ISSN: 0022-1295.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE

LANGUAGE: English
REFERENCE COUNT: 48
"ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS"
AB The voltage-dependent potassium channel, ***Kv1*** . ***3*** , is modulated by the epidermal growth factor receptor (EGFr) and the insulin receptor tyrosine kinases. When the EGFr and ***Kv1*** . ***3*** are coexpressed in HEK 293 cells, acute treatment of the cells with EGF during a patch recording can suppress the ***Kv1*** . ***3*** current within tens of minutes. This effect appears to be due to tyrosine phosphorylation of the channel, as it is blocked by treatment with the tyrosine kinase inhibitor erbstatin, or by mutation of the tyrosine at channel amino acid position 479 to phenylalanine. Previous work has shown that there is a large increase in the tyrosine phosphorylation of ***Kv1*** . ***3*** when it is coexpressed with the EGFr. Pretreatment of EGFr and ***Kv1*** . ***3*** cotransfected cells with EGF before patch recording also results in a decrease in peak ***Kv1*** . ***3*** current. Furthermore, pretreatment of cotransfected cells with an ***antibody*** to the EGFr ligand binding domain (alpha-EGFr),which blocks receptor dimerization and tyrosine kinase activation, blocks the EGFr-mediated suppression of ***Kv1*** . ***3*** current. Insulin treatment during patch recording also causes an inhibition of ***Kv1*** . ***3*** current after tens of minutes, while pretreatment for 18 h produces almost total suppression of current. In addition to depressing peak ***Kv1*** . ***3*** current, EGF treatment produces a speeding of C-type inactivation, while pretreatment with the alpha-EGFr slows C-type inactivation. In contrast, insulin does not influence C-type inactivation kinetics. Mutational analysis indicates that the EGF-induced modulation of the inactivation rate occurs by a mechanism different from that of the EGF-induced decrease in peak current. Thus, receptor tyrosine kinases differentially modulate the current magnitude and kinetics of a voltage-dependent potassium channel.

L4 ANSWER 22 OF 34 MEDLINE
ACCESSION NUMBER: 1998022559 MEDLINE
DOCUMENT NUMBER: 98022559
TITLE: Subcellular localization of the K+ channel subunit Kv3.1b in selected rat CNS neurons.
AUTHOR: Sekimjak C; Martone M E; Weiser M; Deerinck T; Bueno E; Rudy B; Ellisman M
CORPORATE SOURCE: Department of Neuroscience, University of California at San Diego, La Jolla 92092, USA.
CONTRACT NUMBER: NS35215 (NINDS)
NS30989 (NINDS)
RR04050 (NCRR)
+
SOURCE: BRAIN RESEARCH, (1997 Aug 22) 766 (1-2) 173-87.
Journal code: B5L. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY WEEK: 19980302
AB Voltage-gated potassium channels constitute the largest group of heteromeric ***ion*** ***channels*** discovered to date. Over 20 genes have been isolated, encoding different channel subunit proteins which form functional tetrameric K+ channels. We have analyzed the subcellular localization of subunit Kv3.1b, a member of the Kv3 (Shaw-like) subfamily, in rat brain at the light and electron microscopic level, using immunocytochemical detection. Detailed localization was carried out in specific neurons of the neocortex, hippocampus and cerebellum. The identity of Kv3.1b-positive neurons was established using double labeling with markers for specific neuronal populations. In the neocortex, the Kv3.1b subunit was expressed in most parvalbumin-containing bipolar, basket or chandelier cells, and in some bipolar or double bouquet neurons containing calbindin. In the hippocampus, Kv3.1b was expressed in many parvalbumin-containing basket cells, as well as in calbindin-positive neurons in the stratum oriens, and in a small number of interneurons that did not stain for either parvalbumin or calbindin. Kv3.1b protein was not present in pyramidal cells in the neocortex and the hippocampus, but these cells were outlined by labeled presynaptic terminals from interneuron axons that surround the postsynaptic cell. In the cerebellar cortex, granule cells were the only population expressing the channel protein. Careful examination of individual granule cells revealed a non-uniform distribution of ***Kv3*** . ***1*** staining on the somata: circular bands of labeling were present in the vicinity of the axon hillock. In cortical and hippocampal interneurons, as well as in cerebellar granule cells, the Kv3.1b subunit was present in somatic and unmyelinated axonal membranes and adjacent cytoplasm, as well as in the most proximal portion of dendritic processes, but not throughout most of the dendrite. Labeling was also seen in the terminals of labeled axons, but not at a higher concentration than in other parts of the axon. The distribution in the cells analyzed supports a role in action potential transmission by regulating action potential duration.

L4 ANSWER 23 OF 34 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:404705 CAPLUS
DOCUMENT NUMBER: 125:49268
TITLE: A high capacity screen for immunoregulants
INVENTOR(S): Boltz, Robert C. Jr.
PATENT ASSIGNEE(S): Boltz, Robert, C., Jr., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610091	A1	19960404	WO 1995-US12316	19950925

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: US 1994-314760 19940929
AB A process for screening for immunoregulant compds. that modulate T cell activation by blocking potassium channel ***Kv1*** . ***3*** comprises measuring the effect of the immunoregulant compd. on membrane potential by blocking potassium channel ***Kv1*** . ***3*** is claimed. A method for analyzing compds. for activity as immunoregulants using a high capacity screening techniques.

L4 ANSWER 24 OF 34 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:428479 CAPLUS
DOCUMENT NUMBER: 125:76326
TITLE: A high capacity screen for immunoregulants using intracellular calcium concentration measurement
INVENTOR(S): Boltz, Robert C., Jr.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610090	A1	19960404	WO 1995-US12315	19950925

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRIORITY APPLN. INFO.: US 1994-314755 19940929
AB A process is provided for obtaining reproducible intracellular calcium concn. measurements for immunoregulants, which depolarize the membrane potential of human T cells by blocking potassium channel ***Kv1*** . ***3*** . A method is provided for analyzing compds. for activity as immunoregulants using the reproducible intracellular calcium concn. measurement in a high capacity screening technique.

L4 ANSWER 25 OF 34 MEDLINE
DUPLICATE 8
ACCESSION NUMBER: 96355376 MEDLINE
DOCUMENT NUMBER: 96355376
TITLE: Tyrosine phosphorylation-dependent suppression of a voltage-gated K+ channel in T lymphocytes upon Fas stimulation.
AUTHOR: Szab`o I; Gulbins E; Apfel H; Zhang X; Barth P; Busch A E; Schlottmann K; Pongs O; Lang F
CORPORATE SOURCE: Physiology Institute I, Eberhard-Karls University, D-72076 Tubingen, Germany.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Aug 23) 271 (34) 20465-9.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199612
AB Selective cell death plays a critical role in the development of the immune system and in the elimination of target cells expressing foreign antigens. Most of programmed cell death occurs by apoptosis. Apoptotic cell death of lymphocytes can be triggered by ligation of APO-1/Fas (CD95) antigen (Suda, T., and Nagata, S. (1994) J. Exp. Med. 179, 873-879; Nagata, S., and Golstein, P. (1995) Science 267, 1449-1456). We find that activation of Fas leads to the inhibition of the voltage-dependent n-type K+ channels (***Kv1*** . ***3***) studied by patch clamp technique in Jurkat T lymphocytes. Tyrosine kinases have been shown to be crucial in Fas-induced cell death (Eischen, C. M., Dick, C. J., and Leibson, P. J. (1994) J. Immunol. 153, 1947-1954). The inhibition of the current is correlated with the tyrosine phosphorylation of immunoprecipitated and blotted K+ channel protein. We show, that the Src-like protein-tyrosine kinase inhibitor herbimycin A and the deficiency of the p56(lck) tyrosine kinase in mutant Jurkat cells abolished the channel inhibition and phosphorylation by anti-Fas ***antibody*** , while reconstitution of the p56(lck) kinase partly restored these effects of Fas receptor triggering. These results suggest a regulation of n-type K+ channels by tyrosine kinases upon Fas receptor triggering, which might be important for apoptosis.

L4 ANSWER 26 OF 34 BIOSIS COPYRIGHT 2001 BIOSIS
DUPLICATE 9
ACCESSION NUMBER: 1996:159729 BIOSIS
DOCUMENT NUMBER: PREV199698731864
TITLE: Tyrosine phosphorylation of the ***Kv1*** . ***3*** potassium channel.
AUTHOR(S): Holmes, Todd C.; Fadool, Debra A.; Levitan, Irwin B. (1)
CORPORATE SOURCE: (1) Volen Cent. Complex Systems, Grad. Dep. Biochem., Brandeis University, Waltham, MA 02254 USA
SOURCE: Journal of Neuroscience, (1996) Vol. 16, No. 5, pp. 1581-1590.
ISSN: 0270-6474.

DOCUMENT TYPE: Article
LANGUAGE: English
AB ***Kv1*** . ***3*** , a voltage-dependent potassium channel cloned
from mammalian brain and T lymphocytes, contains multiple tyrosine
residues that are putative targets for tyrosine kinases. We have examined
the tyrosine phosphorylation of ***Kv1*** . ***3*** , expressed
transiently in human embryonic kidney (or HEK) 293 cells, by endogenous
and coexpressed tyrosine kinases. Tyrosine phosphorylation is measured by
a strategy of immunoprecipitation followed by Western blot analysis, using
antibodies that specifically recognize ***Kv1*** . ***3***
and phosphotyrosine. Coexpression of the constitutively active tyrosine
kinase v-src, together with ***Kv1*** . ***3*** , causes a large
increase in the tyrosine phosphorylation of the channel protein. This
phosphorylation of ***Kv1*** . ***3*** can be reversed by treatment
with alkaline phosphatase before Western blot analysis. Coexpression with
a receptor tyrosine kinase, the human epidermal growth factor receptor,
also causes an increase in tyrosine phosphorylation of ***Kv1*** .
3 . The effects of endogenous tyrosine kinases were examined by
treating ***Kv1*** . ***3*** -transfected cells with the specific
membrane-permeant tyrosine phosphatase inhibitor pervanadate. Pervanadate
treatment causes a time- and concentration-dependent increase in the
tyrosine phosphorylation of ***Kv1*** . ***3*** . This increased
tyrosine phosphorylation of ***Kv1*** . ***3*** is accompanied by a
time-dependent decrease in ***Kv1*** . ***3*** current, measured by
patchclamp analysis with cell-attached membrane patches. The
pervanadate-induced suppression of current and much of the channel
tyrosine phosphorylation are eliminated by mutation of a specific tyrosine
residue, at position 449 of ***Kv1*** . ***3*** , to phenylalanine.
Thus, there is a continual phosphorylation and dephosphorylation of
Kv1 . ***3*** by endogenous kinases and phosphatases, and
perturbation of this constitutive phosphorylation/dephosphorylation cycle
can profoundly influence channel activity.

L4 ANSWER 27 OF 34 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 96:891987 SCISEARCH
THE GENUINE ARTICLE: VU959
TITLE: Generation and characterization of subtype-specific
monoclonal ***antibodies*** to K+ channel alpha- and
beta-subunit polypeptides
AUTHOR: BekeleArcuri Z; Matos M F; Manganas L; Strassle B W;
Monaghan M M; Rhodes K J; Trimmer J S (Reprint)
CORPORATE SOURCE: SUNY STONY BROOK, DEPT BIOCHEM & CELL BIOL, STONY BROOK,
NY 11794 (Reprint); SUNY STONY BROOK, DEPT BIOCHEM & CELL
BIOL, STONY BROOK, NY 11794; SUNY STONY BROOK, INST CELL &
DEV BIOL, STONY BROOK, NY 11794; WYETH AYERST RES, DEPT
CNS DISORDERS, PRINCETON, NJ 08543
COUNTRY OF AUTHOR: USA
SOURCE: NEUROPHARMACOLOGY, (JUL 1996) Vol. 35, No. 7, pp. 851-865.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD,
LANGFORD LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB.
ISSN: 0028-3908.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 43
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Molecular characterization of mammalian voltage-sensitive K+ channel
genes and their expression became possible with the cloning of the Shaker
locus of Drosophila. However, analysis of the expression patterns and
subunit composition of native K+ channel protein complexes requires
immunological probes specific for the individual K+ channel gene products
expressed in excitable tissue. Here, we describe the generation and
characterization of monoclonal ***antibodies*** (mAbs) against eight
distinct mammalian K+ channel polypeptides; the Kv1.1, ***Kv1*** .
2 , Kv1.4, Kv1.5 and Kv1.6 Shaker-related alpha-subunits, the Kv2.1
Shab-related alpha-subunit, and the Kv beta 1 and Kv beta 2 beta-subunits.
We characterized the subtype-specificity of these mAbs against native K+
channels in mammalian brain and against recombinant K+ channels expressed
in transfected mammalian cells. In addition, we used these mAbs to
investigate the cellular and subcellular distribution of the corresponding
polypeptides in rat cerebral cortex, as well as their expression levels
across brain regions. Copyright (C) 1996 Elsevier Science Ltd

L4 ANSWER 28 OF 34 MEDLINE
DUPLICATE 10
ACCESSION NUMBER: 97072815 MEDLINE
DOCUMENT NUMBER: 97072815
TITLE: Ultrastructural localization of Shaker-related potassium
channel subunits and synapse-associated protein 90 to
septate-like junctions in rat cerebellar Pinceaux.
AUTHOR: Laube G; Roper J; Pitt J C; Sewing S; Kistner U; Garner C
C; Pongs O; Veh R W
CORPORATE SOURCE: Zentrum fur Molekulare Neurobiologie, Universitat Hamburg,
Germany.. laube@plexus.uke.uni-hamburg.de
SOURCE: BRAIN RESEARCH. MOLECULAR BRAIN RESEARCH, (1996 Nov) 42 (1)
51-61.
Journal code: MBR. ISSN: 0169-328X.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY WEEK: 19970505
AB The Pinceau is a paintbrush-like network of cerebellar basket cell axon
branchlets embracing the initial segment of the Purkinje cell axon. Its
electrical activity contributes to the control of the cerebellar cortical
output through the Purkinje cell axon by generating an inhibitory field
effect. In addition to the structural features of the Pinceau, its
repertoire of voltage-gated ***ion*** ***channels*** is likely to
be an important aspect of this function. Therefore, we investigated the
fine structural distribution of voltage-activated potassium (Kv1.1,
Kv1 . ***2*** , Kv3.4) and sodium channel proteins in the
Pinceau. The ultrastructural localization of potassium channel subunits
was compared to the distribution of synapse-associated protein 90 (SAP90),
a protein capable to induce in vitro clustering of Kv1 proteins. With an
improved preembedding technique including ultrasmall gold particles,
silver enhancement and gold toning, we could show that ***antibodies***
recognizing Kv1.1, ***Kv1*** . ***2*** and SAP90 are predominantly
localized to septate-like junctions, which connect the basket cell axonal
branchlets. Kv3.4 immunoreactivity is not concentrated in junctional
regions but uniformly distributed over the Pinceau and the pericellular
basket surrounding the Purkinje cell soma. In contrast, voltage-activated
sodium channels were not detected in the Pinceau, but localized to the
Purkinje cell axon initial segment. The results suggest that Kv1.1 and
Kv1 . ***2*** form heterooligomeric delayed rectifier type Kv
channels, being colocalized to septate-like junctions by interaction with
SAP90.

L4 ANSWER 29 OF 34 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:828710 CAPLUS
DOCUMENT NUMBER: 123:220607
TITLE: [125I]Margatoxin, an Extraordinarily High Affinity
Ligand for Voltage-Gated Potassium Channels in
Mammalian Brain
AUTHOR(S): Knaus, Hans-Guenther; Koch, Robert O. A.; Eberhart,
Andreas; Kaczorowski, Gregory J.; Garcia, Maria L.;
Slaughter, Robert S.
CORPORATE SOURCE: Institute for Biochemical Pharmacology, Innsbruck,
A-6020, Austria
SOURCE: Biochemistry (1995), 34(41), 13627-34
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Monoiodotyrosine margatoxin ([125I]MgTX) specifically and reversibly
labels a max. of 0.8 pmol of sites/mg of protein in purified rat brain
synaptic plasma membrane vesicles with a dissocn. const. of 0.1 pM under
equil. binding conditions. This Kd value was confirmed by kinetic expts.
(Kd of 0.07 pM), competition assays employing native margatoxin (MgTX) (Ki
of 0.15 pM), and receptor satn. studies (Kd of 0.18 pM). Thus, this toxin
represents the highest affinity, reversible radioligand for any
membrane-bound receptor or ***ion*** ***channel*** described to
date. [125I]MgTX binding in this system is modulated by charybdotoxin (Ki
of 5 pM), kaliotoxin (Ki of 1.5 pM), and the agitoxins I and II (Ki's of
0.1 and 0.3 pM, resp.), in a noncompetitive manner. Moreover,
.alpha.-dendrotoxin displayed a Ki value of 0.5 pM. Iberiotoxin was
without any effect, suggesting that the receptor site is likely to be
assocd. with a voltage-gated K+ channel complex. [125I]MgTX binding is
inhibited by cations that are established blockers of voltage-dependent K+
channels (Ba2+, Ca2+, Cs+). The monovalent cations Na+ and K+ stimulate
binding at low concns. before producing complete inhibition as their
concns. are increased. Stimulation of binding results from an allosteric
interaction that decreases Kd, whereas inhibition is due to an ionic
strength effect. Affinity labeling of the binding site in rat brain
synaptic plasma membranes employing [125I]MgTX and the bifunctional
crosslinking reagent, disuccinimidyl suberate, causes specific and
covalent incorporation of toxin into a glycoprotein of an apparent mol.
wt. (Mr) of 74 000. Deglycosylation studies reveal an Mr for the core
polypeptide of the MgTX receptor of 63 000. Immunopptn. studies,
employing sequence-directed ***antibodies*** indicate that at least
Kv1 . ***2*** and ***Kv1*** . ***3*** are integral
constituents of the rat brain MgTX receptor.

L4 ANSWER 30 OF 34 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:747833 CAPLUS
DOCUMENT NUMBER: 123:140316
TITLE: Thalamocortical projections have a K+ channel that is
phosphorylated and modulated by cAMP-dependent protein
kinase
AUTHOR(S): Moreno, Herman; Kentros, Clifford; Bueno, Earl;
Weiser, Michael; Hernandez, Arturo; de Miera, Eleazar
Vega-Saenz; Ponce, Arturo; Thornhill, William; Rudy,
Bernardo
CORPORATE SOURCE: Department Physiology Neuroscience, New York
University Medical Center, New York, NY, 10016, USA
SOURCE: J. Neurosci. (1995), 15(8), 5486-501
CODEN: JNRSDS; ISSN: 0270-6474

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The finding that some K+ channel mRNAs are restricted to certain
populations of neurons in the CNS suggests that there are K+ channels
tailored to certain neuronal circuits. One such example are the
transcripts from the KV3.2 gene, the majority of which are expressed in
thalamic relay neurons. To gain insights into the specific roles of KV3.2
subunits, site specific ***antibodies*** were raised to det. their
localization in thalamic relay neurons. Immunohistochem. and focal
lesioning studies demonstrate that KV3.2 proteins are localized to the
terminal fields of thalamocortical projections. It is also shown that
KV3.2 channels expressed in vitro are strongly inhibited through
phosphorylation by cAMP-dependent protein kinase (PKA). Channels contg.
KV3 . ***1*** subunits, which otherwise exhibit nearly identical
electrophysiol. properties in heterologous expression systems but have a
different and less restricted pattern of expression in the CNS, are not
affected by PKA. Therefore, this modulation might be assocd. with the
specific roles of KV3.2 subunits. Furthermore, it was demonstrated that
KV3.2 proteins can be phosphorylated in situ by intrinsic PKA. KV3.2
subunits display properties and have a localization consistent with a role
in the regulation of the efficacy of the thalamocortical synapse, and
could thereby participate in the neurotransmitter-mediated control of
functional states of the thalamocortical system assocd. with global states
of awareness.

L4 ANSWER 31 OF 34 MEDLINE
DUPLICATE 11
ACCESSION NUMBER: 95348839 MEDLINE
DOCUMENT NUMBER: 95348839
TITLE: Association and colocalization of K+ channel alpha- and
beta-subunit polypeptides in rat brain.
AUTHOR: Rhodes K J; Keilbaugh S A; Barrezueta N X; Lopez K L;
Trimmer J S
CORPORATE SOURCE: Department of CNS Biological Research, Lederle
Laboratories, American Cyanamid Company, Pearl River, New
York 10965, USA..
SOURCE: JOURNAL OF NEUROSCIENCE, (1995 Jul) 15 (7 Pt 2) 5360-71.
Journal code: JDF. ISSN: 0270-6474.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
AB Recent cloning of auxiliary subunits associated with voltage-gated
ion ***channels*** and their subsequent coexpression with the
channel forming alpha-subunits has revealed that the expression level,
gating and conductance properties of the expressed channels can be
profoundly affected by the presence of an auxiliary subunit polypeptide.
In the present study, we raised ***antibodies*** against the
beta-subunit associated with the bovine dendrotoxin sensitive K(+)-channel
complex and used these ***antibodies*** to characterize the related
beta-subunit polypeptides in rat brain. The anti-beta-subunit
antibodies displayed a specific reaction on immunoblots of rat
brain membranes with a major 38 kDa polypeptide, and a minor 41 kDa
polypeptide, which correspond closely to the predicted sizes of the Kv
beta 2 and Kv beta 1 beta-subunit polypeptides, respectively, recently
cloned from rat brain. Reciprocal coimmunoprecipitation experiments
revealed that the beta-subunit polypeptides are associated with
Kv1 . ***2*** and Kv1.4, but not Kv2.1, alpha-subunits.
Immunohistochemical staining revealed that the beta-subunit polypeptides
were widely distributed in adult rat brain. Moreover, the cellular
distribution of beta-subunit immunoreactivity corresponded closely with
immunoreactivity for ***Kv1*** . ***2*** , and to a lesser extent
Kv1.4, but not with Kv2.1. These results suggest that neuronal mechanisms
may exist to direct the selective interaction of K+ channel alpha- and
beta-subunit polypeptides, and that the properties of K+ channels in
specific subcellular domains may be regulated by the formation of
heteromultimeric K+ channel complexes containing specific combinations of
alpha- and beta-subunits.

L4 ANSWER 32 OF 34 MEDLINE
DUPLICATE 12
ACCESSION NUMBER: 95339592 MEDLINE
DOCUMENT NUMBER: 95339592
TITLE: Differential expression of voltage-gated K+ channel
subunits in adult rat heart. Relation to functional K+
channels?.
AUTHOR: Barry D M; Trimmer J S; Merlie J P; Nerbonne J M
CORPORATE SOURCE: Department of Molecular Biology and Pharmacology,
Washington University School of Medicine, St Louis, Mo
63110, USA.
SOURCE: CIRCULATION RESEARCH, (1995 Aug) 77 (2) 361-9.
Journal code: DAJ. ISSN: 0009-7330.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
AB Polyclonal ***antibodies*** against each of the K+ channel subunits (
Kv1 . ***2*** , Kv1.4, Kv1.5, Kv2.1, and Kv4.2) shown previously
to be expressed in adult rat heart at the mRNA level were used to examine
the distributions of these K+ channel subunits in adult rat atrial and
ventricular membranes. Immunohistochemistry on isolated adult rat
ventricular myocytes revealed strong labeling with the anti-Kv4.2 and
anti- ***Kv1*** . ***2*** ***antibodies*** . Although somewhat
weaker (than with anti- ***Kv1*** . ***2*** or anti-Kv4.2), positive
staining was also observed with the anti-Kv1.5 and anti-Kv2.1
antibodies . Ventricular myocytes exposed to the anti-Kv1.4
antibody , in contrast, did not appear significantly different from
background. Qualitatively similar results were obtained on isolated adult
rat atrial myocytes. Western blots of atrial and ventricular membrane
proteins confirmed the presence of ***Kv1*** . ***2*** , Kv1.5,
Kv2.1, and Kv4.2 and revealed differences in the relative abundances of
these subunits in the two membrane preparations. Kv4.2, for example, is
more abundant in ventricular than in atrial membranes, whereas ***Kv1***
. ***2*** and Kv2.1 are higher in atrial membranes; Kv1.5 levels are
comparable in the two preparations. In contrast to these results, nothing
was detected in Western blots of atrial or ventricular membrane proteins
with the anti-Kv1.4 ***antibody*** at concentrations that revealed
intense labeling of a 97-kD protein in adult rat brain membranes. A very
faint band was detected at 97 kD in the atrial and ventricular
preparations when the anti-Kv1.4 ***antibody*** was used at a 5- to
10-fold higher concentration. The simplest interpretation of these results
is that Kv1.4 is not an abundant protein in adult rat atrial or
ventricular myocytes. Therefore, it seems unlikely that Kv1.4 plays an
important role in the formation of functional depolarization-activated K+
channels in these cells. The relation(s) between the (other four) K+
channel subunits and the depolarization-activated K+ channels identified
electrophysiologically in adult rat atrial and ventricular myocytes is
discussed in the present study.

L4 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:130310 CAPLUS
DOCUMENT NUMBER: 120:130310
TITLE: ***Antibodies*** specific for distinct Kv subunits
unveil a heterooligomeric basis for subtypes of
.alpha.-dendrotoxin-sensitive potassium channels in
bovine brain
AUTHOR(S): Scott, Victoria E. S.; Muniz, Zilda M.; Sewing,
Sabine; Lichtinghagen, Ralf; Parcej, David N.; Pongs,
Olaf; Dolly, J. Oliver
CORPORATE SOURCE: Department of Biochemistry, Imperial College, London,
SW7 2AY, UK
SOURCE: Biochemistry (1994), 33(7), 1617-23
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authentic subunit compns. of neuronal K+ channels purified from bovine
brain were analyzed using a monoclonal ***antibody*** (mAb 5),
reactive exclusively with the ***Kv1*** . ***2*** subunit of the
latter and polyclonal ***antibodies*** specific for fusion proteins
contg. C-terminal regions of 4 mammalian Kv proteins. Western blotting of
the K+ channels isolated from several brain regions, employing the
selective blocker .alpha.-dendrotoxin (.alpha.-DTX), revealed the presence
in each of 4 different Kvs. Variable amts. of Kv1.1 and 1.4 subunits were
obsd. in the K+ channels purified from cerebellum, corpus striatum,
hippocampus, cerebral cortex, and brain stem; contents of Kv1.6 and 1.2
subunits appeared uniform throughout. Each Kv-specific ***antibody***
pptd. a different proportion (anti- ***Kv1*** . ***2*** > 1.1 >> 1.6
> 1.4) of the channels detectable with radioiodinated .alpha.-DTX in every
brain region, consistent with a widespread distribution of these
oligomeric subtypes. Such heterooligomeric combinations were further
documented by the lack of additivity upon their pptn. with a mixt. of
antibodies to Kv1.1 and ***Kv1*** . ***2*** ; moreover,
cross-blotting of the multimers pptd. by mAb 5 showed that they contain
all 4 Kv proteins. Evidently, subtypes of .alpha.-DTX-susceptible K+
channels are prevalent throughout mammalian brain which are composed of
different Kv proteins assembled in complexes, shown previously to also
contain auxiliary .beta.-subunits.

L4 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:167431 CAPLUS
DOCUMENT NUMBER: 118:167431
TITLE: Immunological identification of the Shaker-related
Kv1 . ***3*** potassium channel protein in T
and B lymphocytes, and detection of related proteins
in flies and yeast
AUTHOR(S): Spencer, Robert H.; Chandy, K. George; Gutman, George
A.
CORPORATE SOURCE: Dep. Microbiol., Univ. California, Irvine, CA, 92717,
USA
SOURCE: Biochem. Biophys. Res. Commun. (1993), 191(1), 201-6
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Shaker-related potassium (K+) channel proteins contain sequences which
exhibit remarkable conservation across species. The authors have
generated polyclonal anti-peptide ***antibodies*** (Abs) which
cross-react with peptide epitopes of several Shaker-related channels

(Kv1.1, 1.2 and 1.3), in addn. to a ***Kv1*** . ***3*** -specific Ab.

The ***Kv1*** . ***3*** -specific Abs react with a protein expressed in human T-cells (Jurkat and PBLs), as well as in mouse T-cells (EL-4) and pre-B cells (230.37). The cross-reactive Abs detect the Shaker protein in Drosophila melanogaster, in addn. to an immunol. related protein in the yeast Saccharomyces cerevisiae. Abs which recognize these shared epitopes could serve for the identification and biochem. characterization of Shaker-related proteins in diverse organisms.